

From the INTERNATIONAL SEARCHING AUTHORITY

PCTNOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT
OR THE DECLARATION

(PCT Rule 44.1)

To:

MINTZ, LEVIN, COHN, FERRIS
GLOVSKY AND POPEO, P.C.
Attn. ELRIFI, Ivor R.
One Financial Center
Boston, MA 02111
UNITED STATES OF AMERICA

Date of mailing
(day/month/year)

17/01/2001

Applicant's or agent's file reference

15966-562

FOR FURTHER ACTION

See paragraphs 1 and 4 below

International application No.

PCT/US 00/ 24220

International filing date

(day/month/year)

31/08/2000

Applicant

CURAGEN CORPORATION

1. ☒ The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patenilaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Mireille Claudepierré
AN 2 3 2001

RECEIVED

MINTZ LEVIN, BOSTON
PATENT DOCKET DEPT.

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments and any accompanying statement, under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the time of filing the amendments (and any statement) with the International Bureau, also file with the International Preliminary Examining Authority a copy of such amendments (and of any statement) and, where required, a translation of such amendments for the procedure before that Authority (see Rules 55.3(a) and 62.2, first sentence). For further information, see the Notes to the demand form (PCT/IPEA/401).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 15966-562	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 00/ 24220	International filing date (day/month/year) 31/08/2000	(Earliest) Priority Date (day/month/year) 03/09/1999
Applicant CURAGEN CORPORATION		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☒ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

A. CLASSIFICATION OF SUBJECT

IPC 7 C12N15/12 N15/85 C07K14/705 C07K16 C12Q1/68
 G01N33/50 G01N33/53 A61K38/17

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K C12Q G01N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, STRAND

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 00 68266 A (BECKER GERALD WAYNE ;JOHNSTONE EDWARD MARION (US); LITTLE SHEILA P) 16 November 2000 (2000-11-16) page 7 -page 9 page 14 -page 17 SEQ ID NO 2 and 4	1-25,27
P,X	WO 99 46281 A (BAKER KEVIN P ;CHEN JIAN (US); GENENTECH INC (US); GURNEY AUSTIN () 16 September 1999 (1999-09-16) page 12, line 10 - line 22 claim 12; figure 51 figure 50	1-25,27

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

12 January 2001

Date of mailing of the international search report

17. 01. 01

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Blanco Urgoiti, B

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0068266	A	16-11-2000	NONE	

WO 9946281	A	16-09-1999	AU 3072199 A	27-09-1999
			AU 3075099 A	11-10-1999
			EP 1064382 A	03-01-2001
			WO 9947677 A	23-09-1999
			AU 1532499 A	15-06-1999
			EP 1032667 A	06-09-2000
			WO 9927098 A	03-06-1999
			AU 3757099 A	08-11-1999
			WO 9954467 A	28-10-1999
			AU 1070399 A	10-05-1999
			EP 1025227 A	09-08-2000
			WO 9920756 A	29-04-1999

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

ELRIFI, Ivor R.
MINTZ, LEVIN, COHN, FERRIS
GLOVSKY AND POPEO, P.C.
One Financial Center
Boston, MA 02111
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ATP

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MINTZ LEVIN, BOSTON
PATENT DOCKET DEPT.

PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT
(PCT Rule 71.1)

+1 617 542 2241

Date of mailing
(day/month/year)

24.01.2002

Applicant's or agent's file reference
15966-562

IMPORTANT NOTIFICATION

International application No.
PCT/US00/24220

International filing date (day/month/year)
31/08/2000

Priority date (day/month/year)
03/09/1999

Applicant
CURAGEN CORPORATION

Done By
Jhm
1/24
☒ Data Entry
☒ Docket Entry
☐ Docket Cross Off
☐ Previously Entered
☐ No Docketing Req.
☐ ELITE
☐ Annuities

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/

 European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer

Guerin, A

Tel. +49 89 2399-8061



PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 15966-562	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/24220	International filing date (day/month/year) 31/08/2000	Priority date (day/month/year) 03/09/1999
International Patent Classification (IPC) or national classification and IPC C12N15/12		
Applicant CURAGEN CORPORATION		



- This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 11 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☒ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 03/04/2001	Date of completion of this report 24.01.2002
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Moonen, P Telephone No. +49 89 2399 8538 

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/24220

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-81 as originally filed

Claims, No.:

1-26 as originally filed

Drawings, sheets:

1/13-13/13 as originally filed

Sequence listing part of the description, pages:

1-43, filed with the letter of 07.11.2000

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☒ furnished subsequently to this Authority in written form.
☒ furnished subsequently to this Authority in computer readable form.
☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/24220

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

II. Priority

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:
- ☐ copy of the earlier application whose priority has been claimed.
 - ☐ translation of the earlier application whose priority has been claimed.
2. ☒ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid.

Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:
see separate sheet

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
- ☐ the entire international application.
 - ☒ claims Nos. 16-17 and 25-26.

because:

- ☒ the said international application, or the said claims Nos. 16-17 and 25-26 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/24220

- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
- ☐ the computer readable form has not been furnished or does not comply with the standard.

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.
- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☒ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☒ not complied with for the following reasons:
see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☐ all parts.
- ☒ the parts relating to claims Nos. concerning SEQ ID NO:1 and 2.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims 4-26
	No: Claims 1-3
Inventive step (IS)	Yes: Claims

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/24220

No: Claims 4-26
Industrial applicability (IA) Yes: Claims 1-15, 18-24
No: Claims

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Reference is made to the following documents:

- D1:** WO 99 46281 (BAKER KEVIN P ;CHEN JIAN (US); GENENTECH INC (US); GURNEY AUSTIN, 16 September 1999 (1999-09-16)
- ~~**D2:** WO 00 68266 A (BECKER GERALD WAYNE ;JOHNSTONE EDWARD MARION (US); LITTLE SHEILA P) 16 November 2000 (2000-11-16)~~
- D3:** Freemam et al. J Exp Med **174** (1991) 625-31 (abstract) *
- D4:** Zhang & Johnson Cell Immunol **10** (1997) 9-17 (abstract) *
- D5:** Nishimura et al. Eur J Immunogen **27** (Oct-Dec 2000) 427-430; cited as an expert opinion *
- D6:** Swallow et al. Immunity **11** (Oct 1999) 423-26 (**intermediate document**) *
- D7:** Amino acid sequence comparison concerning SEQ ID NO:6 and Pro352 of D1*
- D8:** Amino acid sequence comparison concerning SEQ ID NO:1 and Pro352 of D1*
- D9:** Dong et al. Nature Medicine **5** (December 1999) 1365 (**intermediate document**)*
- D10:** Ling et al. J Immunol (15 Feb 2000) 1653 (**intermediate document**) *

The documents D3-D10 were not cited in the international search report. Copies of the documents have been supplied to the Applicant.

Introduction

1. The B7 proteins are B-cell activation-antigens, divided into B7-1 (**CD80**) and B7-2 (**CD86**). The encoding CD80 sequences have been cloned: see e.g. human (**D3**), rhesus macaque (see **D4**) and also as summarized in the experts opinion **D5** from cattle (Parsons & Howard, 1999), rabbits (Isono & Seto, 1995) and rats (Maeda et al. 1997) and the encoding sequences of CD86 from human (Freeman et al. 1993b), pigs (Mahet et al. 1996), rabbits (Isono & Seto, 1995) and mice (Freeman et al, 1993a). **CD80 and CD86 have** amino acid sequences that are about 25% identical mainly in the **immunoglobulin V- and C-like extracellular domains**. Other members of the B7 family have also been disclosed in the priority interval of P1 and P2 (see **D1** and **D6**). **D9-D10** are other intermediate documents concerning a BLAA polypeptide.

Intermediate document **D1** discloses a cDNA sequence of a novel butyrophilin homolog designated **PRO352** (description page 12, section 21 and claim 12),

indicated also to have **regions of identity to immunoglobulins** and MHC (see Figure 51). A part of SEQ ID NO:6 of the present application (encoded by the cDNA of SEQ ID NO:5) overlaps with 97.9 % of an amino sequence of PRO352 (see the attached sequence comparison D7) and the N-terminal start of both sequences are also identical. D1 also discloses overlapping sequences with SEQ ID NO:2 and NO:4 (e.g. for present SEQ ID NO:2 starting with residues TGALEV-- (Thr- residue 50), and in PRO353 starting with Thr-residue 27).

2. The present application is based on the discovery of BLAA polynucleotide sequences encoding potentially novel members of the human B7 family and provides the nucleotide and amino acid sequences (which method was followed for the provision of the sequences does not appear to have been indicated in the specification). Homology with butyrophilin and myelin oligodendrocyte glycoprotein is also noted (description page 5 lines 9-11).

Re Item II

Priority

3. Only SEQ ID NO:1 and 2 are entitled to the priority date of P1; for the other sequences D1 and D6 (both publication dates in September and October 1999 are between the filing dates of P1 and P2) are therefore fully citable against SEQ ID NO:3-6 as prior art documents.

All priority documents including P1 are much more limited in their disclosure than the presently examined invention referring largely to unsupported subject-matter. P1 (filing date 03 September 1999) discloses the discovered sequences ID NO:1 and 2; furthermore, it is disclosed that protein sequence homology studies revealed 20-25% identity to human butyrophilin, as well as to human myelin oligodendrocyte glycoprotein and members of the B7 family of molecules; the new protein is most likely localized in the membrane of the endoplasmatic reticulum.

The subject-matter of all claims on file goes beyond the disclosure of P1 and the right of priority to P1 is therefore denied for all claims.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

4. For the assessment of the present claims 16-17 and 25-26 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Claims 16-17 and 25-26 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item IV

Lack of unity of invention

5. In view of the lack of priority-entitlement of SEQ ID NO:3-6 on P1 and the availability of D1 (for the disclosure see above; the disclosure of **D1 is prejudicial to the novelty of claim 10** when referring to SEQ ID NO:6) and D6 (concerning the provision of another member of the B7 family, making also the search for additional human members obvious) as prior art documents, the present International Preliminary Examining Authority considers that the claimed subject-matter, e.g. the three different nucleotide sequences SEQ ID NOs:1, 3 and 5, is not linked by a special feature; the three identified inventions in the present application are:
- i. **Claims referring to SEQ ID NO:1 and 2 and depending claims;**
 - ii. **Claims referring to SEQ ID NO:3 and 4 and depending claims;**
 - iii. **Claims referring to SEQ ID NO:5 and 6 and depending claims.**

It is considered that a single general inventive concept (referred to in Rule 13 PCT and the PCT Preliminary Examination Guidelines Ch.III, 7) is not recognisable in the absence of a common, special technical feature.

6. The Applicant decided not to respond to the invitation to pay additional fees or to restrict the application: **the IPER is established for the first mentioned invention** (concerning SEQ ID NO:1 and 2).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

7. The search report refers to the following parts of D1: page 12, section 21 referring to **PRO 352** identified as a novel **butyrophilin homolog**. The amino acid sequence of PRO 352 is given in Figure 51, and is identical to the present SEQ ID NO:2, except for the first N-terminal 25 residues.

A sequence comparison, as made in D8, indicates a 95,7% identity in a 1553 nt overlap of SEQ ID NO:1 and PRO352 of D1. Therefore, the present application does not satisfy the criterion set forth in Article 33(2) PCT because the subject-matter of **claims 1-3** is not new in respect of prior art as defined in the regulations (Rule 64(1)(3) PCT). D1 does not refer to an oligonucleotide of less than 100 nucleotides: however D1 discloses stretches of 100 nucleotides having full identity: **claim 6** does not involve an inventive step, contrary to the requirements of Art. 33(3) PCT.

8. The amino acid sequences of SEQ ID NO:2 and PRO352 are not fully identical and differ in particular at the N-terminus. However, the involvement of an inventive step is denied for the subject matter related directly to full length sequence of SEQ ID NO:2; the noted difference is only considered to result from different experimental set-ups. No special properties have been demonstrated to exist for SEQ ID NO:2. Therefore, the present application does not satisfy the criterion set forth in Article 33(3) PCT because the subject-matter of **claims 4-5 and 10-11** does not involve an inventive step (Rule 65(1)(2) PCT).

9. The features of directly or indirectly dependent **claims 7-9, 12-26** are based on similar products and methods employed for the same purpose in the prior art. It would therefore be obvious to the person skilled in the art, to produce or develop methods corresponding to this prior art, thereby arriving at the subject-matter according to claims 7-9 and 12-26.
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Re Item VI

Certain published documents (Rule 70.10)

Certain published documents (Rule 70.10)

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
D2	16.11.00	09.05.2000	11.05.1999

10. D2 (WO 00/68266), when valid claiming priority, may be of importance during the regional european phase with respect to novelty under Article 54(3)(4) EPC).

Re Item VII

Certain defects in the international application

11. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1, D6 and D9-D10 is not mentioned in the description, nor are these documents identified therein.
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Re Item VIII

Certain observations on the international application

12. In conjunction with the above observations, it is noted that Article 6 of the PCT requires that all independent claims contain the essential technical feature(s) of the invention (see also Rule 6.3(a) PCT).

You are therefore invited to indicate in your response to this opinion the special technical feature of the invention, present in all independent claims on file.

EXAMINATION REPORT - SEPARATE SHEET

13. Claim 12 as well as the claims concerning the medical use lack sufficient support and/or disclosure (Articles 5 and 6 PCT). Given the family ties with other known proteins it is unclear how an antibody that selectively binds has to be produced. Furthermore, no examples mention a demonstrated positive result in a medical treatment.
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PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE
 in its capacity as elected Office

Date of mailing (day/month/year) 20 June 2001 (20.06.01)	Applicant's or agent's file reference 15966-562
International application No. PCT/US00/24220	Priority date (day/month/year) 03 September 1999 (03.09.99)
International filing date (day/month/year) 31 August 2000 (31.08.00)	
Applicant GREEN, Cynthia et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
 03 April 2001 (03.04.01)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Charlotte ENGER Telephone No.: (41-22) 338.83.38
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PATENT COOPERATION TREATY

PCT

From the INTERNATIONAL BUREAU

NOTIFICATION RELATING TO PRIORITY CLAIM

(PCT Rules 26bis.1 and 26bis.2 and
Administrative Instructions, Sections 402 and 409)

To:

ELRIFI, Ivor, R.
Mintz, Levin, Cohn, Ferris,
Glovsky and Popeo, P.C.
One Financial Center
Boston, MA 02111
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 16 February 2001 (16.02.01)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference 15966-562	
International application No. PCT/US00/24220	International filing date (day/month/year) 31 August 2000 (31.08.00)
Applicant CURAGEN CORPORATION et al	

The applicant is hereby notified of the following in respect of the priority claim(s) made in the international application.

1. ☒ **Correction of priority claim.** In accordance with the applicant's notice received on: 23 October 2000 (23.10.00), the following priority claim has been corrected to read as follows:
US 30 August 2000 (30.08.00) 09/651,200
 - ☐ even though the indication of the number of the earlier application is missing.
 - ☐ even though the following indication in the priority claim is not the same as the corresponding indication appearing in the priority document:
2. ☐ **Addition of priority claim.** In accordance with the applicant's notice received on: , the following priority claim has been added:
 - ☐ even though the indication of the number of the earlier application is missing.
 - ☐ even though the following indication in the priority claim is not the same as the corresponding indication appearing in the priority document:
3. ☐ As a result of the correction and/or addition of (a) priority claim(s) under items 1 and/or 2, the (earliest) priority date is:
4. ☐ **Priority claim considered not to have been made.**
 - ☐ The applicant failed to respond to the Invitation under Rule 26bis.2(a) (Form PCT/IB/316) within the prescribed time limit.
 - ☐ The applicant's notice was received after the expiration of the prescribed time limit under Rule 26bis.1(a).
 - ☐ The applicant's notice failed to correct the priority claim so as to comply with the requirements of Rule 4.10.

The applicant may, before the technical preparations for international publication have been completed and subject to the payment of a fee, request the International Bureau to publish, together with the international application, information concerning the priority claim. See Rule 26bis.2(c) and the PCT Applicant's Guide, Volume I, Annex B2(1B).
5. ☐ In case where multiple priorities have been claimed, the above item(s) relate to the following priority claim(s):
6. A copy of this notification has been sent to the receiving Office and
 - ☐ to the International Searching Authority (where the international search report has not yet been issued).
 - ☒ the designated Offices (which have already been notified of the receipt of the record copy).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. (41-22) 740.14.35	Authorized officer Marie-José Devillard Telephone No. (41-22) 338.83.38
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